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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,093	DALY, JOHN	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/28/06.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25,27-44 and 46-145 is/are pending in the application.

4a) Of the above claim(s) 1-22,29,43,59-67,69-84 and 103-106 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 23-25,27,28,30-41,46-58,68,85-90,93,94,96-100 and 107-145 is/are rejected.

7)☒ Claim(s) 42,44,91,92 and 95 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 5/24/06 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 2/28/06. Claims 5, 13, 26, 27, 45, 62, 65, 69-72, 101 and 109 have been cancelled. Claims 1, 14-20, 23, 54-58, 60, 61, 63, 64, 66, 68, 81, 83, 93, 94, 103, 105, 110 and 133 have been amended. Claims 1-4, 6-12, 14-25, 28-44, 46-61, 63, 64, 66-68, 73-100, 102-108 and 110-145 are pending in this application. Claims 1-4, 6-12, 14-22, 29, 43, 59-61, 63, 64, 66-68, 73-84 and 103-106 have been withdrawn. Therefore, claims 23-25, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are under examination in the application.

It is noted that the amendment includes text for cancelled claims. To be totally compliant with 37 CFR 1.21, the text of canceled claims should not be included. However, in order to expedite prosecution of this case, the requirement for compliance was waived.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. The new grounds of rejection herein were necessitated by amendment and, therefore, this action is final.

Claim Objections

Claims 24, 25, 28, 30-42, 44, 46-53, 54-58, 85-92, 95-100, 102, 107-145 are objected to because of the following informalities: the claims refer to "a construct according to claim" which should correctly be -- the construct according to claim --. By recitation of "a construct",

the claims indicate that there are more than one constructs in the independent claims and the dependent claims refer to one of the constructs". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 102 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Claim 102 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The term "cells" defined by the specification at page 8, line 3-12 states that the cell is *in vitro* or *in vivo*. The scope of the claims, therefore encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "non-human" or "isolated" would be remedial.

Response to Argument

Applicants have argued that the claims have been amended to overcome the rejection under 35 USC 101. However, applicants' have not amended claim 102.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 68 and 107-145 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by applicants' amendment.**

Claims 68 and 107-145 are vague and indefinite in that the metes and bounds of "a polynucleotide that encodes a comprising a protein-destabilizing element" are unclear. It appears as if applicants did not intend to delete the word "polypeptide". However, by its deletion, the claim is unclear.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-25, 28, 30-42, 46-58, 68, 87-90, 96-100, 107, 108, 110-123, 125-137 and 140-143 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Applicants recite a construct that comprises a genus of RNA elements that modulate the stability of a transcript.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, applicants recite a construct for assaying the activity of a gene expression-modulating element or for identifying elements of this type or agents that modulate their activity. The construct comprises in operable linkage a polynucleotide that encodes a polypeptide having an intracellular half-life of less that about 3 hours, a nucleic acid that encodes an RNA element that modulates the stability of a transcript encoded by the polynucleotide. The specification teaches that specific RNA elements are typically rich in the nucleotide bases AU and are typically found in the 3' UTR of a gene. Specifically, the specification teaches a variety of these genes and discloses several elements that function to modulate transcript stability such as from *c-fos* and found in SEQ ID NO:19. It is unclear if all 3' UTR sequences comprise the elements required to modulate stability or simply a subset of these genes such as those disclosed. While numerous RNA elements are found in nature, it is unclear whether any of these elements modulate stability as in the instantly recited claims. Neither the prior art nor the specification teaches that any of these elements mediate RNA stability. Given the large size and diverse nature of "RNA elements" and the inability to determine which will also possess the ability to

modulate the stability of a transcript in a construct, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on pages 21-24 of the amendment filed 2/28/2006. Applicants argue that the elements are not limited to those isolated from the 3'UTR but also include those that are synthetic and from the 5' UTR of genes. Specifically, applicants point to the specification discloses synthetic AU rich elements and Shyu et al (previously considered) discloses that *c-fos* contains two destabilizing elements in the 3'UTR and the coding sequence of the *c-fos* gene. Newman et al (previously disclosed) discloses examples of 5'UTR destabilizing elements. As well, applicants argue that the specification defines "RNA destabilizing elements as a sequence of nucleotides which reduces the intracellular half-life of a RNA transcript" and provides examples by listing genes from which these elements can be isolated. Specifically, the specification discloses SEQ ID NO:s 1-23 that are RNA destabilizing elements. It is applicants' position that these sequences are known and the written description requirement should not require a teaching as to the structural variation across the genus of RNA destabilizing elements when it is clear that the art is replete with nucleic acid sequences.

Applicants' arguments filed 2/28/06 have been fully considered but they are not persuasive. These arguments have focused on the occurrence of AU rich elements outside of the

3'UTR of genes. However, the claims are not limited to AU-rich elements. In fact, the Written Description requirement for the instant claims is based upon the recitation of "RNA destabilizing elements" as it encompasses a broad and diverse collection of sequences that only require that they be nucleic acid capable of destabilizing RNA. Applicants only disclose a species of RNA elements that destabilize the stability of a transcript that are AU rich elements or U rich elements as disclosed in SEQ ID NO:s 1-23. The sequences outside of this species of elements are not known and the art is not replete with the nucleic acid sequences of elements that are not AU-rich. Hence, applicants have not demonstrated that they are in possession of any elements that are "RNA destabilizing elements" except AU-rich or U rich destabilizing elements, which reduce the stability of the transcript.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 68, 107-118, 120-122, 125, 126, 129-135, 138 and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao et al (Methods in Enzymology, 1999, Vol 302, pages 32-38; see entire document) as evidenced by Eurekah Bioscience (Eurekah.com, Degradation of RNA in prokaryotes) further as evidenced by Kessler et al (NAR, 1986, p. 4939-4952; see entire

document). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Zhao et al teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. page 33, paragraph 1) operably linked to a SV40 polyadenylation sequences, a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide (see e.g. figure 4). The polyadenylation sequence leads to destabilization of the transcript as evidenced by Eurekah et al (see e.g. paragraph 1) as recited in claim 107. The components of the construct of Zhao et al are demonstrated in the instant specification to be functional in assaying the activity of a gene expression-modulating element as recited in claim 68 and 116. The polyadenylation sequence and the polynucleotide are heterologous to one another as recited in claim 108. The polynucleotide encodes a polypeptide that comprises GFP, which functions to emit light and as a selection marker, that is destabilized by introduction of the mouse ornithine decarboxylase degradation domain, and a PEST sequence, as recited in claims 109-113, 121, 125, 126 and 140. The construct comprises a *Bgl*II site in operable connection with the polynucleotide and the nucleic acid sequence (see e.g. page 34, paragraph 3, which describes insertion of NF-kB binding sites in frame with GFP at a *Nhe*I-*Bgl*II site) as recited in claim 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. figure 4) as recited in claim 117, 118 and 120. The vector is inserted into human cells (see e.g. page 35, paragraph 2) as recited in claims 133-135. The SV40 polyadenylation sequence comprises an AU rich element as evidenced by Kessler et al (see e.g. abstract) as recited in claims 138.

Claims 68, 93, 94, 96-100, 102, 107-118, 120-122, 125, 126, 129-136, 138 and 140-145 are rejected under 35 U.S.C. 102(a) as being anticipated by Leclarc et al (Biotechniques, 2000, Vol 29, pages 590-601; see entire document) as evidenced by Eurekah Bioscience (Eurekah.com, Degradation of RNA in prokaryotes) further as evidenced of Kessler et al (NAR, 1986, p. 4939-4952; see entire document) and further as evidenced by Clontech (pMAMneo map, downloaded 9/14/05). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Leclerc et al teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. abstract) operably linked to SV40 polyadenylation, a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide (see e.g. page 591, col 2, last paragraph as evidenced by the map for pMAM-neo). The components of the construct of LeClerc et al are demonstrated in the instant specification to be functional in assaying the activity of a gene-expression modulating element as recited in claim 68 and 116. The polyadenylation sequence leads to destabilization of the transcript as evidenced by Eurekah et al (see e.g. paragraph 1) as recited in claim 107. The polyadenylation sequence and the polynucleotide are heterologous to one another as recited in claim 108. The polynucleotide encodes a polypeptide that comprises luciferase, which functions to emit light and as a selection marker, and the mouse ornithine decarboxylase degradation domain, which contains a PEST sequence (see e.g. page 590, col 2-3) as recited in claims 109-113, 121, 125, 126 and 140-143. The construct comprises a multiple cloning site in operable connection with the polynucleotide and the nucleic acid sequence (see e.g. map, pMAMneo) as recited in claim 114, 115, 122 and

129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. map pMAMneo) as recited in claim 117, 118 and 120. The vector is inserted into a cell (see e.g. page 591, col 1, paragraph 2) as recited in claims 133-136. The SV40 polyadenylation sequence comprises an AU rich element as evidenced by Kessler et al (see e.g. abstract) as recited in claims 93, 94, 96-100, 102, 138, 144 and 145.

Claims 23-25, 28, 30-37, 39-41, 46, 47, 50-55, 68, 85, 87, 107-118, 120-122, 125, 126, 129-134, 138 and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) as evidenced by Wach et al (Yeast, 1997, page 1065-1075; see entire document) as evidenced by Wach et al (Yeast, 1994, p. 1793-1808; see entire document) further as evidenced by Bennetzen and Hail, JBC, 1982, p. 30183025; see entire document) as evidenced by Eurekah Bioscience (Eurekah.com, Degradation of RNA in prokaryotes). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Mateus and Avery teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. abstract) operably linked to a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide, ADH1 terminator. The construct does not contain a promoter but contain a multiple cloning site for insertion of gene expression modulating elements (see e.g. page 1314, col 2, last paragraph as evidenced by Wach et al, 1997, figure 4). The ADH1 terminator encodes the polyadenylation sequence as evidenced by Wach et al (1994, page 1795, col 1, paragraph 3, which as evidenced by Eurekah et al leads to destabilization of the

transcript (see e.g. paragraph 1) as recited in claim 24, 35 and 107. As demonstrated in the instant specification, such a construct is functional in assaying the activity of a gene-expression modulating element as recited in claim 23, 68 and 116. The termination sequence and the polynucleotide are heterologous to one another as recited in claims 25 and 108. The polynucleotide encodes a polypeptide that comprises GFP, which functions to emit light and as a selection marker, and a PEST sequences at the C-terminus (see e.g. page 1314, col 2, last paragraph) as recited in claims 27, 28, 30-32, 46, 47, 87, 109-113, 121, 125, 126 and 140. The construct comprises a multiple cloning site in operable connection with the polynucleotide and the nucleic acid sequence for the insertion of promoter sequences or for linearization or for insertion of other elements (see e.g. page 1314, col 2, last paragraph as evidenced by Wach et al, 1997, figure 4) as recited in claim 33, 34, 41, 50-53, 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. Wach et al, figure 4) as recited in claim 36, 37, 40, 117, 118 and 120. The vector is inserted into a cell (see e.g. page 591, col 1, paragraph 2) as recited in claims 39, 54, 55, 133-134. As evidenced by Bennetzen et al. the termination sequence and polyadenylation sequence of ADH1 comprises an AU rich element (see e.g. figure 4) as recited in claim 85 and 138.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Li and Kain (US 6,130,313; see entire document). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Applicants claim a construct comprising a polynucleotide and a nucleic acid that encodes an RNA element that modulates stability of a transcript and a site for introducing a gene expression-modulating element and a translational enhancer in mammalian and human cells.

The teachings of Mateus and Avery are as above except:

Mateus and Avery do not teach that the methods of assaying promoters using a destabilized reporter can be used in human and mammalian cells.

Li and Kain et al teach methods of use of rapidly degrading GFP fusion constructs for use in analyzing regulatory elements and/or cis-acting regulatory elements. Li and Kain et al teach that these constructs comprise a GFP coding sequence fused to a mouse ornithine decarboxylase coding sequence in a vector. Li and Kain do not explicitly teach that the vectors lack promoters and comprise a sequence that encodes a RNA element that modulates the stability of the transcript.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the vector of Mateus and Avery in mammalian and human cells as taught by Li and Kain because Mateus and Avery, teach that it is within the ordinary skill of the art to generate a vector comprising GFP-pest for analysis of gene expression in cells and because Li and Kain teach that such a vector can be used in human and mammalian cells to analyze regulatory elements. One would have been motivated to do so in order to receive the expected

benefit of promoterless vectors with destabilized transcripts and proteins to insert the regulatory elements to be examined as taught by Li and Kain. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 48, 49, 127 and 128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Methods in Enzymology, 1999, Vol 302, pages 32-38; see entire document) or Leclarc et al (Biotechniques, 2000, Vol 29, pages 590-601; see entire document) or Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Primig et al (Gene, 1998, Vol 215, pages 181-189; see entire document). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Applicants claim a construct comprising a chimeric gene comprising a coding sequence from a gene encoding a light emitting protein and a selectable marker protein and a nucleic acid sequence that encodes a RNA element that modulates the stability of a transcript encoded by the chimeric gene. The polypeptide encoded by the polynucleotide is a chimeric gene such as comprising genes encoding light emitting protein and a selectable marker protein.

The teachings of Zhao et al, Leclerc et al and Mateus and Avery are described above and are applied as before except:

Neither Zhao et al, Andersen et al, Leclerc et al and Mateus nor Avery teach that the reporter is a chimeric gene encoding comprising genes encoding light emitting protein and a selectable marker protein.

Primig et al teach use of a reporter gene that is a fusion between GFP and neomycin phosphotransferase (see e.g. page 183, bridging paragraph col 1-2). The cited benefits of the vector were localization of reporter and selection functions in one gene decreasing chances of undesirable recombination events, reducing false positives, optimal conditions for identifying gene expression modulators (see e.g. bridging paragraph page 187-188).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the separate reporter and selectable marker genes taught by Zhao et al, and Mateus and Avery with the GFP-neo fusion taught by Primig et al because Zhao et al, Leclerc et al and Mateus and Avery teach that it is within the ordinary skill of the art to generate a vector comprising a destabilized reporter gene for analysis of gene expression in cells and because Primig et al teach that it is within the ordinary skill of the art to use GFP-neo as a reporter gene in cells. One would have been motivated to do so in order to receive the expected benefit of localization of reporter and selection function sin one gene decreasing chances of undesirable recombination events, reducing false positives, optimal conditions for identifying gene expression modulators (see Primig et al, bridging paragraph page 187-188). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 38 and 119 are rejected under 35 U.S.C. 103(a) as being unpatentable Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Svensson and

Akusjarvi (EMBO J. 1985, Vol 4, No. 4, pages 957-964; see entire document). **This rejection is maintained for reasons of record in the office action mailed 9/27/05 and restated below.**

Applicants claim a construct comprising a polynucleotide and a nucleic acid that encodes an RNA element that modulates stability of a transcript and a site for introducing a gene expression-modulating element and a translational enhancer.

The teachings of Mateus and Avery are described above and are applied as before except:

Mateus and Avery do not teach that the vector further comprises a translational enhancer.

Svensson and Akusjarvi teach the use of adenovirus VA RNAI on the translation of mRNAs. The expression was elevated 2-6 fold (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add to the vector of Mateus and Avery, the VA RNAI translation enhancer taught by Svensson and Akusjarvi because Mateus and Avery, teach that it is within the ordinary skill of the art to generate a vector comprising a reporter gene for analysis of gene expression in cells and because Svensson and Akusjarvi teach that it is within the ordinary skill of the art to include a translational enhancer in a vector. One would have been motivated to do so in order to receive the expected benefit of enhanced reporter activity to identify low signaling events or elements that modulate these events. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 102 and 103 on pages 24-26 of the amendment filed 2/28/06. Applicants argue that the SV40 polyadenylation site does not lead to RNA destabilization in eukaryotic cells but are used in eukaryotic cells because it generates high yields of RNA and protein. Secondly, applicants argue that the art does not teach a nucleic acid sequence that encodes a RNA element as the polyadenylation signal does not encode a poly(A) tail but is a signal that recruits enzymes to cleave the RNA and add the poly(A) tail.

Applicants' arguments filed 2/28/06 have been fully considered but they are not persuasive. The instant claims are drawn to a construct comprising in operable linkage a polynucleotide sequence encoding a polypeptide with a destabilizing element and a *nucleic acid encoding an RNA element that modulates stability of the transcript*, which are taught in the prior art. It is applicants' contention that a polyadenylation sequences does not meet the requirements of an RNA element that modulates stability of a transcript by destabilizing the transcript because 1) it does not destabilize RNA in eukaryotes and 2) it does not encode a poly(A)tail. The claims simply recite that the nucleic acid encodes an RNA element that modulates stability of the transcript. As such, the polyadenylation signal is nucleic acid that modulates the stability of RNA or transcripts to which it is attached in light of the teachings of Eurekah, "Polyadenylation has since been shown to be involved in the degradation of other species of RNA and of RNA in general". Secondly, the online dictionary defines encode to mean "to carry the genetic information that enables a polypeptide, RNA molecule, or one of their constituent groups to be produced". Based

upon this definition, the nucleic acid encodes a polyadenylation signal, which is responsible according to Eurekah for modulating the stability of a transcript.

Conclusion

Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER